

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/050415

International filing date (day/month/year)
01.02.2005

Priority date (day/month/year)
04.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D401/04, C07D401/14, A61K31/497, A61P11/00

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITYInternational application No.
PCT/EP2005/050415

10/587836

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:
see separate sheet

Box No. III Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 17, 18

because:

- ☒ the said international application, or the said claims Nos. 17, 18 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/050415

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	1-18
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-16
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/050415

10/587836**Re Item I****Basis of the opinion**

The application is directed to

- (i) 2-(piperidin-4-yl)-pyridazin-3-ones (1) (claims 1-13),
- (ii) the medical use of compounds (1) (claim 14),
- (iii) a pharmaceutical composition comprising a compound (1) (claim 15),
- (iv) the second medical use of compounds (1) (claim 16), and
- (v) the corresponding therapeutic methods (claims 17-18).

Re Item II**Priority**

The claimed date of priority does not appear valid for compounds (I) wherein R²² and R²³ together form ring systems selected from morpholin-3,5-dione-4-yl to isoindol-1,3-dione-2-yl according to claim 1, the claims 2-13, and subject matter referring to these compounds respectively claims.

Re Item III**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 17 and 18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1 Reference is made to the following documents.

D1: EP-A-0 738 715, 23.10.1996; cited in the application.

D2: WO 02/064584 A, 22.08.2002; cited in the application.

D3: WO 02/085906 A, 31.10.2002; cited in the application.

D4: WO 2004/018449 A, 04.03.2004.

D4 was published after the priority date. Under the presumption that the priority is valid for the claimed matter the said document is not considered as prior art under Rule 64.1 PCT.

2 Novelty

2.1 **D1** relates to pyridazinone derivatives as PDE4 inhibitors. The present compounds (1) differ from the compounds of **D1** through the 1-R⁹-piperidin-4-yl group and in having the R¹/R² alkyl groups in position 4 rather than in position 5. The present claimed matter is thus novel vis-à-vis **D1**.

D2 and **D3** relate to phthalazinone derivatives as PDE4 inhibitors. The present compounds (1) differ from the compounds of **D2/D3** insofar as they represent monocyclic pyridazinones rather than bicyclic phthalazinones. The present claimed matter is thus novel vis-à-vis **D2/D3**.

2.2 The P-document **D4** relates also to phthalazinones as PDE4 inhibitors, whereas the application is directed to pyridazines. **D4** will, thus, not become relevant to the question of novelty of the application.

4 Inventive Step

4.1 The application describes the preparation of certain compounds (1) and shows that such compounds exhibit PDE4 inhibitory activity (the application, page 34).

4.2 In view of **D1** as most relevant state of the art the problem underlying the application may be seen in the provision of further PDE4 inhibitors. The present compounds (1) differ from those of **D1** in bearing in the 2-position a 1-R⁹-piperidin-4-yl substituent rather than a group -Q-R⁵ and in bearing the two R¹/R² alkyl substituents in position 4 instead of 5. Although the documents **D2** and **D3** teach already that the present R⁹-piperidin-4-yl substituents are compatible with the desired activity, it does not appear

unequivocally obvious in view of the cited prior art that the additional structural modification concerning the position of the alkyl groups R¹/R² would lead to further compounds of PDE4 inhibitory activity. Hence, based on the activity of the tested examples, the subject matter of claims 1-18 appears to meet the requirements of inventive step.

4 Industrial Applicability

For the assessment of the present claims 17 and 18 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 2004/018449 A1	04.03.2004	06.08.2003	10.08.2002

Re Item VIII

Certain observations on the international application

Present claim 17 is to be objected under Article 6 PCT, because the therapeutic method is functionally defined by a mechanism of action which does not allow any practical application in the form of a defined, real treatment of a pathological condition. The objection could be overcome by either introducing in the claims a list of pathological conditions (diseases) cited in the application, or by showing that means are available which would allow the skilled person to recognise which additional conditions would fall within the functional definition.